UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/869,176	06/26/2001	Nilgun E. Tumer	OCIRS-072	2863

530 7590 02/07/2003

LERNER, DAVID, LITTENBERG,
KRUMHOLZ & MENTLIK
600 SOUTH AVENUE WEST
WESTFIELD, NJ 07090

EXAMINER	
MEHTA, ASHWIN D	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 02/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/869,176	TUMER ET AL.	
	Examiner	Art Unit	
	Ashwin Mehta	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *24-27 and 32-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23 and 28-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3 and 5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-20, 22, and 28-31 in Paper No. 7 is acknowledged. The traversal is on the ground(s) that Applicants submit that the "exogenous nucleic acid encoding an L3 protein" is a special technical feature that is also common to claims 21-23, 25, 26, and 28-31. This is not found persuasive because the method of Group III encompasses non-plant cells, which are not shared with the method of the claims of Group I. During the course of examination, it was determined that examination of claims 21 and 23 would not impose an undue burden, and Group II was rejoined with Group I. Claims 1-23 and 28-31 have been examined in this office action. Claims 24-27 and 32-35 are withdrawn as being drawn to non-elected inventions.

The requirement is still deemed proper and is therefore made FINAL.

Specification

2. Page 32, lines 38-39 cite U.S. Patent No. 5,880,322 for describing wild type PAP, PAP-*v*, and various PAP mutants. However, this patent does not describe these proteins, but rather teaches a method to produce diarylmethanes. Correction/clarification is required. New matter must be avoided.

Claim Objections

3. Claims 6 and 28 are objected for the following reasons:

Claim 6 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form. Claim 6 attempts to limit claim 1 by requiring the nucleic acid to encode a wild-type L3 protein. However, claim 1 does not mention anything that suggests that mutant L3 proteins are encompassed. The specification does not define "L3" as a name that refers to both wild type and mutant versions of a protein. It is not conventional in the art to refer to both the wild type and mutants versions of a protein with the same designation, as this obviously would cause great confusion. Claim 6 then does not further limit claim 1. In the interest of expediting prosecution, claim 1 will be examined hereinafter as if the exogenous nucleic acid encodes either a wild type or mutant L3 protein (except for the rejection of claims 7-11 under 35 U.S.C. 112, 2nd paragraph, below).

In claim 28: in line 1, "nucleid" is misspelled.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-23 and 28-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1, 12, and 28: the recitation "L3" renders the claims indefinite. The recitation does not clearly identify the intended protein, as numerous different types of proteins may have

such a designation. It is suggested that the term --ribosomal-- be inserted into the claims before "L3".

In claims 7-11: the claims are indefinite because they broaden the scope of parent claim 1. Claims 7-11 attempt to limit claim 1 by requiring the L3 protein to be a mutant. However, as discussed above, claim 1 does not make any mention of mutants, and mutant versions of proteins and genes are not referred to in the art by the same designation given to the wild type protein or gene.

In claims 8, 10, and 11: the recitations "tcm1," "rpl3-I282T," and "Mak8 (W255C, P257S)" in claims 8, 10 and 11, respectively, render them indefinite. These designations do not clearly identify the L3 mutant protein. These designations do not clearly identify the intended mutant protein. The name appears to have been arbitrarily assigned and can be changed. The specific characteristics associated therewith can also be modified. It is suggested that claims 8 and 11 be amended to recite the sequence identifiers of the tcm1 and Mak8 (W255C, P275S) sequences mentioned on pages 18 and 24. Further, page 28 refers to an L3 mutant protein that comprises an "I282T" mutation. However, the specification refers to this protein with a different designation, "rpl-T845C." To clearly identify the intended protein, it is suggested that claim 10 be amended to recite the sequence identifier that sets forth the sequence of rpl-T845C, if this is the same protein referred in the claim as rpl3-I282T.

In claim 13: the article "a" in the recitation "a PAP protein, PAP-*v*, or a PAP II protein" in line 2 renders the claim indefinite. "PAP" is the abbreviation for a particular protein, the pokeweed antiviral protein (specification, page 3, lines 10-13). PAP-*v* is a mutant of PAP, and PAP II is a second pokeweed antiviral protein. These are particular wild type and mutant

versions of a protein from pokeweed taught in the prior art. It is then not clear, because of the article "a" in the recitation, what other PAP, PAP-v, or PAP II proteins are encompassed by the claim.

In claims 17, 18, 20, and 22: the recitation "the nucleic acid of claim 1" or "the exogenous nucleic acid of claim 1" renders the claims indefinite. Claim 1 is directed to a transgenic plant, not a nucleic acid.

In claims 21 and 23: the recitation "the first and second exogenous nucleic acids of claim 12" in lines 2-3 of the claims render them indefinite. Claim 12 is directed to a transgenic plant, not exogenous nucleic acids.

In claim 28: the claim indicates that a mutant L3 protein "(b) is unable to maintain M1 killer virus". Proteins do not have the property of maintaining viruses.

Further in claim 28: the recitation "substantially fails" in line 2 renders the claim indefinite. It is not exactly clear what is meant by "substantially." The term makes the metes and bounds of the claim unclear.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-23 and 28-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn towards any transgenic plant containing any exogenous nucleic acid encoding any L3 protein; or said plant wherein said nucleic acid is derived from any yeast, higher plant, or animal; or said plant wherein said nucleic acid encodes any spontaneously or non-naturally occurring L3 mutant; or wherein said transgenic plant further comprises a second exogenous nucleic acid, encoding any single chain ribosome inhibitory protein (RIP) that binds any endogenous L3 protein; a method of preparing a plant having increased resistance to viruses and/or fungi, comprising introducing said exogenous nucleic acid into a plant cell or protoplast and regenerating a transformed plant; or a method of reducing toxicity of a single chain RIP contained in a plant, comprising introducing exogenous nucleic acids encoding an L3 protein and a single chain RIP; any nucleic acid encoding a non-naturally occurring mutant L3 protein; any cell transformed with said nucleic acid encoding a non-naturally occurring mutant L3 protein.

The specification presents the nucleotide (SEQ ID NO: 1) and corresponding amino acid (SEQ ID NO: 2) sequences of a wild-type yeast L3 protein (pages 6-10), asserts that the prior art teaches L3 nucleic acids cloned from Arabidopsis and rice (page 10, lines 23-25), and presents the nucleotide sequence (SEQ ID NO: 3) and corresponding amino acid sequence (SEQ ID NO: 4) encoding a tobacco L3 protein termed "8d", and the nucleotide sequence (SEQ ID NO: 5) and corresponding amino acid sequence (SEQ ID NO: 6) of a second tobacco L3 protein termed "10d" (page 10, line 25 to page 18, line 36). The specification also presents the nucleotide (SEQ ID NO: 7) and corresponding amino acid (SEQ ID NO: 8) sequences of a spontaneously

occurring mutant L3 gene from *Saccharomyces cerevisae*, termed tcm1 (pages 18-22), the nucleotide (SEQ ID NO: 9) and corresponding amino acid (SEQ ID NO 10) sequences of a mutant yeast L3 allele designated "Mak8 (W255C, P257S)" (pages 24-28), and the nucleotide (SEQ ID NO: 11) and corresponding amino acid (SEQ ID NO: 12) sequences of another mutant L3 allele from yeast, designated "rpl-T845C," in which a nucleotide change results in the conversion of an isoleucine at residue 282 to threonine (I282T; pages 28-32). The specification asserts that pokeweed antiviral protein (PAP), a single-chain ribosome inhibitory protein (RIP), removes a specific adenine residue from the α-sarcin loop of yeast 28S rRNA, thereby preventing binding of eEF-2/GTP complex during translational elongation. PAP binds to the wild-type yeast L3 protein and a mutant L3 protein, Mak8-1p, *in vitro*, but does not depurinate yeast ribosomes comprising the mutant Mak8-1p. Mutant yeast cells comprising ribosomes comprising Mak8-1p are resistant to PAP (Example 1, pages 35-43). The specification also asserts that programmed, -1 ribosomal frameshifting is used by a number of RNA viruses as a means to ensure the correct ratio of viral structural and enzymatic proteins are produced. Altering this ratio interferes with virus propagation, and compounds that alter the kinetics of peptidyl-transfer affect –1 frameshift efficiencies and interfere with virus propagation in yeast (page 43, lines 19-24). M_1 is a yeast virus that requires –1 ribosomal frameshifting to propagate in yeast (page 44, lines 27-33). The specification indicates that the yeast *mak8-1* allele promotes increased programmed –1 ribosomal frameshifting efficiencies and that mutant mak8-1 yeast were unable to maintain the M_1 killer virus (page 48, lines 20-31). The specification also indicates that mutant yeast *mak8-1* cells were not further affected by the peptidyl-transferase inhibitors sparsomycin and anisomycin (page 49, lines 17-26). Further, the specification

indicates that 40 yeast L3 mutants have been produced, but the sequences of only 5 of them have been determined. All 5 had the same mutation, changing the thymidine at position 845 to cytosine, resulting in an isoleucine to threonine substitution at residue 282 (page 58, lines 15-18).

However, the specification does not describe the nucleic acid sequences encoding all L3 proteins of all organisms, as broadly encompassed by the claims. The sequences of the ribosomal L3 proteins set forth in the sequence listing do not provide any information concerning the nucleotide sequences of L3 genes yet to be isolated. However, the specification does not describe any nucleic acid molecules encoding non-naturally occurring mutants of ribosomal L3 proteins other than the yeast tcm1, Mak8 (W255C, P257S), and rpl-T845C. The specification describes the nucleotide bases changes in the wild-type yeast L3 nucleotide sequence that result in the tcm1, Mak8 (W255C, P257S) and rpl-T845C alleles. However, the claims encompass any type of spontaneous or non-naturally occurring mutation of all nucleic acids encoding all L3 proteins of all organisms. No other mutations are described at all. The only structures correlated with a failure to bind single chain RIPS, promoting programmed –1 ribosomal frameshifting efficiency, exhibit resistance to peptidyl-transferase inhibitors, and conferring the inability to maintain M_1 killer virus in yeast are the nucleic acids of tcm1, Mak8 (W255C, P257S), and rpl-T845C, set forth in SEQ ID NOs: 7, 9, and 11. See Fiers vs. Sugarno, 25 USPQ 2d (CAFC 1993) at 1606, which states that "[a]n adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself". Furtherstill, the specification indicates that the P257S point mutation of the yeast mak8 allele was engineered into one of the tobacco L3 genes (page 55, lines 26-27). However, the corresponding amino acid or nucleotide residues in

the tobacco L3 gene are not described. The specification also does not indicate that this mutation in the tobacco L3 protein produced any of the properties listed in claim 28. Furthermore, the specification indicates that the mak8-1 allele had no effect on programmed +1 frameshifting (page 48, lines 32-33). The specification does not describe any L3 mutant that reduces –1 framshifting, or affects +1 or any other programmed ribosomal frameshifting. Regarding claims 8, 10, and 11: as discussed above, it is not clear if the mutant L3 alleles mentioned in these claims are the same as those described on pages 18-22 and 24-32. As discussed above, it is suggested that claims 8, 10, and 11 be amended by inserting the sequence identifiers that set forth the nucleotide sequences that encode the mentioned mutant L3 proteins. Given the breadth of the claims encompassing nucleic acids encoding all mutant L3 proteins, and the lack of written description as discussed above, the specification fails to provide an adequate written description of the multitude of nucleic acid molecules encompassed by the claims.

6. Claims 1-23 and 28-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for transgenic plants containing an exogenous nucleic acid encoding a wild-type L3 protein, nucleic acid molecules encoding the yeast L3 mutants tcm1, Mak8 (W255C, P257S) and rpl1282T set forth in SEQ ID NOs: 8, 10, and 12, respectively, does not reasonably provide enablement for nucleic acid sequences encoding other L3 mutants, or a method of preparing a plant having increased resistance to fungi. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn towards any transgenic plant containing any exogenous nucleic acid encoding any L3 protein; or said plant wherein said nucleic acid is derived from any yeast, higher plant, or animal; or said plant wherein said nucleic acid encodes any spontaneously or non-naturally occurring L3 mutant; or wherein said transgenic plant further comprises a second exogenous nucleic acid, encoding any single chain ribosome inhibitory protein (RIP) that binds any endogenous L3 protein; a method of preparing a plant having increased resistance to viruses and/or fungi, comprising introducing said exogenous nucleic acid into a plant cell or protoplast and regenerating a transformed plant; or a method of reducing toxicity of a single chain RIP contained in a plant, comprising introducing exogenous nucleic acids encoding an L3 protein and a single chain RIP; any nucleic acid encoding a non-naturally occurring mutant L3 protein; any cell transformed with said nucleic acid encoding a non-naturally occurring mutant L3 protein.

As discussed above, the specification asserts that the ribosomal protein, L3, participates in the formation of the peptidyl-transferase center in ribosomes during translation of mRNA. The specification presents the nucleotide (SEQ ID NO: 1) and corresponding amino acid (SEQ ID NO: 2) sequences of a wild-type yeast L3 protein (pages 6-10), asserts that the prior art teaches L3 nucleic acids cloned from Arabidopsis and rice (page 10, lines 23-25), and presents the nucleotide sequence (SEQ ID NO: 3) and corresponding amino acid sequence (SEQ ID NO: 4) encoding a tobacco L3 protein termed "8d", and the nucleotide sequence (SEQ ID NO: 5) and corresponding amino acid sequence (SEQ ID NO: 6) of a second tobacco L3 protein termed "10d" (page 10, line 25 to page 18, line 36). The specification also presents the nucleotide (SEQ ID NO: 7) and corresponding amino acid (SEQ ID NO: 8) sequences of a spontaneously

occurring mutant L3 gene from *Saccharomyces cerevisae*, termed tcm1 (pages 18-22), the nucleotide (SEQ ID NO: 9) and corresponding amino acid (SEQ ID NO 10) sequences of a mutant yeast L3 allele designated "Mak8 (W255C, P257S)" (pages 24-28), and the nucleotide (SEQ ID NO: 11) and corresponding amino acid (SEQ ID NO: 12) sequences of another mutant L3 allele from yeast, designated "rpl-T845C," in which a nucleotide change results in the conversion of an isoleucine at residue 282 to threonine (I282T; pages 28-32). The specification asserts that pokeweed antiviral protein (PAP), a single-chain ribosome inhibitory protein (RIP), removes a specific adenine residue from the α-sarcin loop of yeast 28S rRNA, thereby preventing binding of the eEF-2/GTP complex during translational elongation. The specification teaches that PAP binds to the wild-type yeast L3 protein and a mutant L3 protein, Mak8-1p, *in vitro*, but does not depurinate yeast ribosomes comprising the mutant Mak8-1p. Mutant yeast cells comprising ribosomes comprising Mak8-1p are resistant to PAP (Example 1, pages 35-43). The specification teaches that the yeast *mak8-1* allele promotes increased programmed –1 ribosomal frameshifting efficiencies and that mutant *mak8-1* yeast were unable to maintain the M_1 killer virus (page 48, lines 20-31). The specification also teaches that mutant yeast *mak8-1* cells were not further affected by the peptidyl-transferase inhibitors sparsomycin and anisomycin (page 49, lines 17-26). The specification further teaches that 40 yeast L3 mutants have been produced, but the sequences of only 5 of them have been determined. All 5 had the same mutation, changing the thymidine at position 845 to cytosine, resulting in an isoleucine to threonine. The specification also teaches that tobacco plants transformed with the nucleotide sequence encoding PAP and the yeast L3 gene, both operably linked to the CaMV 35S promoter, had normal phenotypes and showed increased resistance to tobacco mosaic virus (TMV).

Transgenic tobacco plants expressing the yeast *mak8* mutant allele and PAP were also prepared. These plants also showed a higher resistance to TMV versus non-transgenic plants, though not as high as the plants expressing wild-type yeast L3 and PAP (page 56, line 3 to page 57, line 17). Transgenic tobacco plants were also made that were transformed with the tobacco L3 cDNA encoding 8d, in either sense or antisense orientation. Two transgenic plants expressing L3 in sense orientation, and one transgenic line expressing L3 in antisense orientation, showed increased resistance to TMV (page 57, lines 20-25).

However, the specification does not teach the nucleotide sequences encoding any mutant L3 protein other than tcm1, Mak8 (W255C, P257S), and rpl-T845C. The specification indicates that 40 yeast L3 mutants have been produced. However, the specification also admits that only 5 of them have been sequenced, and all of them result in the same amino acid change as in rpl-T845C. See In re Bell, 26 USPQ2d 1529, 1532 (Fed. Cir. 1993) and In re Deuel, 34 UPSQ2d, 1210 (Fed. Cir. 1995), which teach that the mere existence of a protein does not enable claims drawn to a nucleic acid encoding that protein. See also Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016 at 1021 and 1027, (Fed. Cir. 1991) at page 1021, where it is taught that a gene is not reduced to practice until the inventor can define it by "its physical or chemical properties" (e.g. a DNA sequence). The specification does not teach any other mutations of any other ribosomal L3 proteins. In the absence of further guidance, undue experimentation would be required by one skilled in the art to determine all the other mutations of all L3 proteins of all species that would produce the properties enumerated claim 28, or which would confer viral and/or fungal resistance when transgenically expressed in plants, or reduce the toxicity in plants to single chain RIPS.

Further, the specification does not teach any transgenic plants expressing any L3 protein that show increased resistance to any fungus. The only pathogen that plants transgenically expressing the 8d protein have increased resistance against is TMV. As fungi do not require a host plant's ribosomes for propagation, it is not clear why plants transgenically expressing any wild type L8 protein would have increased resistance to fungi. See Genentech, Inc. V. Novo Nordisk, A/S, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention.

Further regarding claim 28: part (d) of the claim encompasses nucleic acids encoding any non-naturally occurring mutant of any L3 protein exhibits resistance to peptidyl-transferase inhibitors. As discussed above, the specification teaches that mutant yeast *mak8-1* cells were not affected by the peptidyl-transferase inhibitors sparsomycin and anisomycin and that wild type L3 proteins participate in the formation of the peptidyl-transferase center of ribosomes. However, it is not clear that it is accurate to say that it is the L3 protein that is susceptible to the peptidyl-transferase inhibitor, rather than the ribosome. The specification does not make clear whether it is the wild type L3 protein that is the target of the peptidyl-transferase inhibitors, versus another protein or ribosomal nucleic acid. For example, the mutant L3 protein may cause a sterical or conformational change to the peptidyl-transferase center such that actual target is no longer affected by peptidyl-transferase inhibitors. If the L3 protein is not the target of the inhibitors, then it is not accurate to say that the mutant L3 protein alone exhibits resistance to the inhibitors, as indicated in the claim. Furtherstill, the specification teaches the effect of expressing the mutant ribosomal L3-encoding nucleotide sequences of the sequence listing in plant and yeast cells. However, the specification does not teach their use in other cell types (other than bacteria,

which are commonly used to store nucleotide sequences of interest or to deliver transgenes to plant cells (Agrobacterium)). It is not clear how one would use the claimed nucleotide sequences in other types of cells. See Genentech, Inc. V. Novo Nordisk, A/S, supra. It is suggested that the cell of claim 29 be limited to plant, bacterial, or yeast cells. Given the breadth of the claims encompassing all spontaneous and non-naturally occurring mutations of any L3 protein, increased resistance against fungi, and nucleic acids encoding L3 mutants that, themselves, exhibit resistance against peptidyl-transferase inhibitors, unpredictability of the art and lack of guidance of the specification, undue experimentation would be required by one skilled in the art to make and use the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

7. Claims 1-5, 7-9, 14-20, 22, and 28-30 rejected under 35 U.S.C. 102(e) as being clearly anticipated by Harris et al. (U.S. Patent No. 6,060,646).

The claims are broadly drawn towards any transgenic plant cell, protoplast, or plant comprising any exogenous nucleic acid encoding any wild type L3 protein or spontaneously or non-naturally occurring L3 mutant protein; or wherein the nucleic acid is derived from a higher plant or animal; or wherein the nucleic acid is heterologous or homologous to the transgenic plant; or wherein the transgenic plant is any monocot, dicot, or cereal; or seed of the transgenic plant; a method of increasing resistance to any virus and/or fungi in any plant, comprising introducing the exogenous nucleic acid into the plant or any nucleic acid encoding a non-naturally occurring mutant L3 protein that (a) substantially fails to bind single chain ribosome inhibitory proteins that bind endogenous L3 proteins, (b) is unable to maintain M1 killer virus, (c) promotes altered programmed ribosomal frameshift efficiency, (d) exhibits resistance to peptidyl-transferase inhibitors and combinations of any of (a)-(d); any cell of any species transformed with the nucleic acid encoding the non-naturally occurring L3 protein.

Harris et al. teach modified nucleic acids of the wild type form of nucleic acids encoding the ribosome L3 protein, including the nucleotide sequence encoding the yeast mutant ribosomal L3 protein tcm1, protoplasts and transgenic plants transformed with the modified nucleic acid, and seeds derived from the transformed plant. Harris et al. modified the wild type L3 genes using site-directed mutagenesis. The transgenic plants may be dicots or monocots, including corn, rye, wheat, barley, and tobacco. Methods of transformation include those in which plant cells are transformed and then regenerated into transformed plants. Protoplasts comprising the

modified nucleic acid were also produced. A transformation vector comprising the modified nucleic acid was introduced into Agrobacterium for the purpose of plant cell transformation. Spontaneously and non-naturally occurring mutants of nucleic acids encoding a ribosomal L3 protein are taught by the reference, as the claims do not limit the modified nucleic acid to be spontaneously or non-naturally occurring. Similarly, Harris et al. teach transgenic plants transformed with the mutant nucleic acid wherein the nucleic acid is heterologous or homologous to the plant, as the claims do not recite any such limitations. The properties of (a) substantially failing to bind single chain ribosome inhibitory proteins that bind endogenous L3 proteins, (b) inability to maintain M1 killer virus, (c) promoting altered programmed ribosomal frameshift efficiency, (d) exhibiting resistance to peptidyl-transferase inhibitors and combinations of any of (a)-(d) are inherent to the modified L3 protein encoded by the modified nucleic acid (col. 6, line 62 to col. 7, line 9; col. 7, lines 18-19; col. 9, line 10 to col. 12, line 46; claims).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1-5, 7-9, 12-23, and 28-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harris et al. (U.S. Patent No. 6,060,646) in combination with Lodge et al.

(Proc. Natl. Acad. Sci., USA, 1993, Vol. 90, pages 7089-7093) and Sambrook et al. (Molecular Cloning A Laboratory Manual Second Edition, 1989, Cold Spring Harbor Press, pages 1.74-1.84).

The claims are broadly drawn towards any transgenic plant containing any exogenous nucleic acid encoding any L3 protein; or said plant wherein said nucleic acid is derived from any yeast, higher plant, or animal; or said plant wherein said nucleic acid encodes any spontaneously or non-naturally occurring L3 mutant; or wherein said transgenic plant further comprises a second exogenous nucleic acid, encoding any single chain ribosome inhibitory protein (RIP) that binds any endogenous L3 protein; a method of preparing a plant having increased resistance to viruses and/or fungi, comprising introducing said exogenous nucleic acid into a plant cell or protoplast and regenerating a transformed plant; or a method of reducing toxicity of a single chain RIP contained in a plant, comprising introducing exogenous nucleic acids encoding an L3 protein and a single chain RIP; any nucleic acid encoding a non-naturally occurring mutant L3 protein; any cell transformed with said nucleic acid encoding a non-naturally occurring mutant L3 protein.

Lodge et al. teach broad-spectrum virus resistance of transgenic plants expressing the single chain inhibitory protein PAP, or a variant PAP (PAP*v*) (pages 7090-7093).

Lodge et al. do not teach transgenic plants expressing a mutant ribosomal L3 protein.

Harris et al. is discussed above. Harris et al. also teach using the modified nucleic acid encoding the mutated ribosomal L3 protein as a selectable marker in plant transformation (col. 8, line 31 to col. 9, line 5; col. 10, line 18 to col.12, line 46; claims).

Sambrook et al. teach a method for transformation of *Escherichia coli*. This reference is cited to address the limitation of claim 31 (pages 1.82 to 1.84).

It would have been obvious and within the scope of one of ordinary skill in the art at the time the invention was made to modify the virus resistant transgenic plants expressing PAP or variant PAP of Lodge et al. by also introducing into the plants the modified nucleic acid encoding the mutant ribosomal L3 protein of Harris et al. It would have been obvious that a transgenic plant expressing both exogenous transgenes would confer virus and fungal resistance to the plant. One would have been motivated to express the PAP and mutant ribosomal L3 proteins together in a transgenic plant, as the proteins would confer the desirable traits of increased virus and fungus resistance to the host plant. One also would have been motivated to transform the exogenous nucleic acid encoding PAP along with the mutant ribosomal L3 protein, given the teaching of Harris et al. that the mutant ribosomal L3 protein can also be used as a selectable marker in plant transformation. It also would have been obvious to transform the modified nucleic acid encoding the mutant ribosomal L3 protein into *E. coli*, for example by following the transformation method taught by Sambrook et al. One would have been motivated to introduce the nucleic acid into *E. coli* as it has been standard practice in the art to store, amplify, and/or express nucleotide sequences of interest in this bacterial cell.

9. Claims 1-23 and 28-31 are rejected.

Contact Information

Any inquiry concerning this or earlier communications from the examiner should be directed to Ashwin Mehta, whose telephone number is 703-306-4540. The examiner can normally be reached on Mondays-Thursdays and alternate Fridays from 8:00 A.M to 5:30 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at 703-306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 and 703-872-9306 for regular communications and 703-872-9307 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

February 3, 2003

ASHWIN D. MEHTA, PH.D
PATENT EXAMINER